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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/820,438	03/29/2001	J. Guy Breitenbacher	ORT-1396	5665

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AUDLEY A. CIAMPORCERO JR.
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

[REDACTED] EXAMINER

LIU, HONG

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1624

DATE MAILED: 03/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 09/820,438	Applicant(s) Breitenbacher et al.
Examiner Hong Liu	Art Unit 1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on _____
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 835 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-32 is/are pending in the application
 4a) Of the above, claim(s) 23-32 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-22 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) Notice of References Cited (PTO-892)
 16) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 17) Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2 and 4

18) Interview Summary (PTO-413) Paper No(s). _____
 19) Notice of Informal Patent Application (PTO-152)
 20) Other: _____

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DETAILED ACTION

Claims 1-32 are pending in this application.

Election/Restriction

Applicants's election of Group I, claims 1-22 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 and 20, 21, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparation and use of compounds wherein R3 is hydrogen or methylsulfonyl, W is O or O-R9, Z is nitrogen-containing heterocycle or NR11R12, does not reasonably provide enablement for preparation and use of compounds wherein R3, W, and Z are skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

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The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein R3, W, and Z can be an unsubstituted or substituted, heteroaromatic group, containing one or more heteroatoms, etc. While many compounds are disclosed, there is insufficient guidance for preparing additional "H3 receptor antagonists" which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein R3 is hydrogen or methylsulfonyl, W is O or O-R9, Z is piperidine, pyrrolidine, pyridine, piperazine, NR11R12 have been made.

Furthermore, testing data is limited to a number of compounds not considered to be representative of all the possible compounds encompassed by the claims. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various R3, W, and Z variables embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the "working examples" fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See *In re Fouch*, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the

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claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability" have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

Furthermore, the instant specification provides no direction or guidance for how to use the disclosed (and claimed) compounds since there are no working examples of experimental data to demonstrate that the compounds affect the function of the respiratory system, no guidelines for determination of dosage needed to reverse obstructive airways disease, no teaching how the data provided permits the determination of an effective amount for treating these disorders,. Therefore, in view of the breadth of the claims, the chemical nature of the invention, the unpredictability of *in vitro* and *in vivo* correlation, the lack of working examples, and the lack of further guidance in how to use the claimed compounds and compositions to actually treat these disorders, it would require an undue amount of experimentation to use the claimed inventions.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1, 9, and 12-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- 1). The use of "heterocyclic" in the definition of R3, W, and Z is unclear to the array of heteroatoms as well as nature of atoms as ring members. See *In re Wiggins* 179 USPQ 421 for certain terminology regarding heterocyclic ring systems.
- 2). Claims 1, 18, 19, and 22 are indefinite in that the metes and bounds of "ester" and "amide" are unknown. There is no definition for these terms in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 10-16, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Chirgadze et al. (WO 98/48797). Chirgadze teaches the compounds and composition of the instant invention (see Examples). *overcome by argument*

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Claims 1, 2, 8, 10-16, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Neuenschwander et al. (5,385,912). Neuenschwander teaches the compounds and composition of the instant invention (see Examples on col. 31). *not overcome a bridged amine is a heterocycle*

Claims 1, 2, 8, 10-16, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Connor et al. (WO 98/06703). Connor teaches the compounds and composition of the instant invention (see Examples on page 24). *not overcome*

Claims 1, 8, 10, 12, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Agarwal et al., Chem Abstract 115: 49618. The instantly claimed compounds read on the reference compound. *not overcome*

Claims 1, 2, 8, 10, 12-16, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Joshi et al., Chem Abstract 105: 190834. The instantly claimed compounds read on the reference compound. *not overcome*

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1, 2, 8, 10-16, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chirgadze et al. (WO 98/48797). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, page 3, wherein R2 is benzyloxy, or X2-(CH2)-NRaRb, R3 is hydrogen, chloro or benzyl group, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render *prima facie* obvious a species falling within a genus. See *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. V. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Claims 1, 2, 8, 10-16, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neuenschwander et al. (US 5,385,912). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, col. 2, wherein Ar I and Ar II are mono-, bicyclic ring, B can be O NR', etc. The compounds are taught

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to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

Claims 1, 2, 8, 10-16, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connor (WO 98/06703). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, page 5, wherein W, X, Y, Z can be C-R2, R1 can be H, lower alkyl, aryl, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would

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have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render *prima facie* obvious a species falling within a genus.

Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (703) 306-5814. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM. If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308-4716. The fax phone number for this group is (703) 308-4734 for "unofficial" purposes and the actual number for **official** business is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose number is (703) 308-1235.

hl
February 18, 2002



RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624
Mukund Shah
Supervisory Patent Examiner
Art Unit 1624